Programmed cell removal by calreticulin in tissue homeostasis and cancer.

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Public Summary:

Scientific Abstract:
Macrophage-mediated programmed cell removal (PrCR) is a process essential for the clearance of unwanted (damaged, dysfunctional, aged, or harmful) cells. The detection and recognition of appropriate target cells by macrophages is a critical step for successful PrCR, but its molecular mechanisms have not been delineated. Here using the models of tissue turnover, cancer immunosurveillance, and hematopoietic stem cells, we show that unwanted cells such as aging neutrophils and living cancer cells are susceptible to "labeling" by secreted calreticulin (CRT) from macrophages, enabling their clearance through PrCR. Importantly, we identified asialoglycans on the target cells to which CRT binds to regulate PrCR, and the availability of such CRT-binding sites on cancer cells correlated with the prognosis of patients in various malignancies. Our study reveals a general mechanism of target cell recognition by macrophages, which is the key for the removal of unwanted cells by PrCR in physiological and pathophysiological processes.